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Increased risk of early-stage breast cancer related to consumption of sweet foods among women less than age 45 in the United States

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Abstract

Objectives: To evaluate the associations of dietary macronutrients, food groups, and eating patterns with risk of breast cancer in a population-based case–control study.
Methods: In this study among women 20–44 years of age, 568 cases with breast cancer and 1451 population-based controls were included. They completed a detailed in-person interview, a self-administered food-frequency questionnaire and were measured for anthropometric indices. Logistic regression was used to estimate odds ratios (OR) and their 95% confidence intervals (CI) of breast cancer, adjusted for age, study site, race, education, alcohol consumption, oral contraceptive usage, smoking status, and body mass index.
Results: There was no association between breast cancer risk and intake of calories, macronutrients, or types of fat. Risk of breast cancer was unrelated to intakes of a variety of food groups, including red meats, dairy, high-fat snacks and desserts, or foods high in animal fat. Increased risk was observed for high intake of a food group composed of sweet items, particularly sodas and desserts. Risk increased linearly with percent of calories from sweets and frequency of sweets intake. Consumption of sweets 9.8 or more times per week compared with <2.8 times per week was associated with an adjusted OR of 1.32 (95% CI = 1.0–1.8). This association did not appear to be due to the high-fat foods or carbonated beverages that comprised the food group. Compared with women reporting one or two meals and snacks per day, reduced risks were noted for women reporting six or more (OR = 0.69, 95% CI = 0.4–1.1).
Conclusions: These data suggest a modest relationship between intakes of sweet items with risk of *in-situ* and localized breast cancer in young women. This relation is consistent with the hypothesized link of high insulin exposure and risk of breast cancer. There was some suggestion that women who ate many times during the day were at reduced risk of disease, which is also consistent with an insulin-related mechanism.

Introduction

Epidemiologic studies have evaluated breast cancer risk in relation to intakes of a variety of dietary factors, particularly dietary fat [1]. Case–control and cohort studies of individuals, however, have not shown consistent results for this macronutrient, and a recent pooled

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analysis of cohort studies showed no association of dietary fat intake and breast cancer risk [2]. Fruit and vegetable intake have also received some attention. A meta-analysis of 26 studies indicated a strong protective effect of vegetables, vitamin C and β-carotene [3]. A comprehensive review of the international literature suggests that fruit and vegetable food groups were associated with reduced risk [4]. A pooled analysis of cohort studies, however, did not find a protective effect of fruit and vegetable consumption for pre- or postmenopausal breast cancer [5]. These studies may have been compromised by low intakes of fruit and vegetables. Thus, it is unclear whether fruit and vegetable intake is associated with reduced risk of breast cancer. Identified risk factors for breast cancer, and particularly premenopausal breast cancer, explain no more than approximately 60% of the disease [6–8]. Therefore, new avenues of research have been pursued to identify additional risk factors that may further explain risk of this disease. Few studies have evaluated aspects of diet beyond those described above, particularly among premenopausal breast cancer patients.

We had the opportunity to evaluate a variety of diet-related factors, with validation data for the food-frequency questionnaire [9], in a large study focused on early-onset breast cancer. Specifically, we evaluated breast cancer risk associated with previously investigated dietary factors, as well as less-studied and novel factors such as types of fat, new food groups, and eating patterns.

Materials and methods

Subjects

This case–control study was conducted in three centers in the United States: Atlanta, GA; Seattle/Puget Sound, WA; and five counties in central New Jersey. Methods for this study have been described in detail elsewhere [10–12]. In brief, between 1 May 1990 and 31 December 1992, cases age 20–44 newly diagnosed with *in-situ* or invasive breast cancer were identified for potential participation in the study through rapid-ascertainment systems. Population-based cancer registries covered all geographic regions, and periodic checks of these registries ensured completeness of patient ascertainment. Controls were frequency-matched by region and age to the expected distribution of cases and were identified through Mitofsky–Waksberg random-digit dialing techniques [13].

Subjects were interviewed regarding demographic factors, reproductive and medical histories, family history of breast cancer, contraceptive behavior, adolescent diet, physical activity, smoking, alcohol consumption, and occupation. As part of the interview, subjects were asked whether they had been diagnosed with breast cancer during the past 12 months, and follow-up questions ascertained what kind of treatment they had received. Anthropometric measurements were taken following the interview [11]. Participants were given a food-frequency questionnaire to complete concerning dietary intake in the past year. Respondents completed this questionnaire while the interviewer was present, or at their leisure, and returned it by mail. Occasionally the questionnaire was completed by telephone interview when receipt of the mailed questionnaire seemed improbable.

Of the 1939 eligible cases, 1668 (86.0%) women were interviewed. The main reasons for nonparticipation were subject refusal (6.6% of eligible cases) and physician refusal (5.8% of cases). A response rate of 90.5% was obtained from the telephone identification screener for random-digit dialing (RDD) controls, resulting in 1912 eligible controls. Of these subjects, 1505 (78.7%) completed interviews. Among eligible case and control subjects, 1632 (84.2%) and 1471 (76.9%), respectively, completed dietary questionnaires. Consideration of the telephone screener rate showed an overall response rate of 69.6% among controls for the dietary questionnaire.

Five controls were removed due to a previous history of breast cancer, and 21 cases without residential telephones were eliminated because of noncomparability with the controls who were identified by RDD techniques. Twenty-three cases and 15 controls were excluded from the analysis because severe errors in their dietary questionnaires were identified through the NCI–Block edit program. Errors included less than three or more than 30 foods consumed per day, more than 15% of food items skipped, and three or more foods with questionably high frequencies. Cases who reported chemotherapy treatment at the time of the interview were found to have had altered reporting of dietary intake and were excluded [14]. There were 1451 controls and 568 cases with *in-situ* or invasive localized disease remaining for analyses.

Dietary data

The dietary questionnaire was a scannable, modified version of the standard 100-item NCI–Block food-frequency questionnaire [15]. Modifications included expansion of questions to differentiate low- and high-fat dairy items, low- and high-caffeine beverages with and without artificial sweeteners, separation of items that

differed in fiber or fat content, added food items relevant to the Atlanta population [16], and an open-ended section to include foods consumed more than once per week that were missing from the food list. The dietary questionnaires were processed using the NCI–Block analysis program (HHHQ-DIETSYS, 1993), version 3.5. We created food groups (see Appendix) using frequency of intake of the line items from the questionnaire as well as of additional food items listed in the open-ended section. Food groups were created to circumvent errors associated with food composition data, and to indirectly address hypotheses related to dietary constituents not available in typical food composition tables. In addition, multiple dietary constituents in whole foods may impart different risk than single nutrients.

Within the NCI–Block analysis program we utilized the program to evaluate the sources or contributors to the food group. This analysis provides, in descending order, the sum of weekly frequencies of each food item for the food group and its percent contribution toward the total frequency for the group. A variable describing servings per week was created by multiplying the frequency by a factor representing servings from the portion size information (Small = 0.5, Medium = 1.0, Large = 2 servings, respectively). Women were also asked how many main meals they usually ate per day, how many snacks (not including beverages alone) they usually ate per day, and how often they usually ate away from home, at a restaurant, cafeteria, or lunch wagon.

Validation data

A validation study was conducted to correct risk estimates for the measurement error associated with the food-frequency questionnaire (FFQ). Methods for the validation study are provided in detail elsewhere [9]. Briefly, all control subjects who completed FFQs in the year prior to the initiation of the validation study created the base population, which was sampled for potential participants for the validation study. This study was conducted over a 1-year period and consisted of six 24-h recalls by telephone and two 3-day records. Two-hundred and two control subjects of the 289 validation subjects were in the analytic sample for the case–control study analyses, which excluded women 45 years of age and older, non-RDD controls, and those with inadequate dietary data.

Statistical analyses

Logistic regression was utilized to estimate odds ratios (OR) and 95% confidence intervals (CI) as measures of the relationships between dietary variables and risk of breast cancer [17]. Quartiles for each dietary factor were defined based on the distribution in the control group. Age in the models was defined as age at date of diagnosis for cases and date of RDD telephone identification screener for controls. Variables considered as potential confounders included study site, race, age at first birth, parity, cigarette smoking, age at menarche, years of oral contraceptive usage, level of education, recent alcohol consumption, history of previous breast biopsy, family history of breast cancer in a first-degree relative, frequency of mammograms in the past five years excluding the past year, and body mass index in kg/m^2 (BMI). The chi-square test of seven key nutrients and potential confounders revealed that the following covariates were related to one or more nutrients and were included in all analyses in addition to age (continuous): site (Atlanta, New Jersey, Seattle), race (white, African-American, other), education (high school, vocational, some college, college graduate, postgraduate), recent alcohol consumption (non-drinker, 1–6.9 drinks/week, 7–13.9 drinks/week, 14+ drinks/week, missing), total duration (lifetime) of oral contraceptive use (0–6 months, 6 months to < 5 years, 5–9 years, 10+ years), smoking (never, past, current), and body mass index (<21.9, 21.9–24.6, 24.7–29.0, >29.0). A continuous variable for calories was added to the models for energy adjustment. Tests for trend in the logistic analyses were obtained by categorizing the exposure variables and treating the scored variables as continuous. Tests for trend were conducted only when there appeared to be a linear trend in the odds ratios.

Correction procedures were used to estimate the attenuation in nutrient risk estimates in the FFQ and correct odds ratios for the observed measurement error. We fit several logistic regression models with continuous dietary covariates and corrected for measurement error using the regression calibration method described in Rosner *et al.* [18], the correction factors being estimated from the validation study. We then compared uncorrected and corrected odds ratios for the nutrients. Each model had two continuous dietary covariates, log (energy) and one macronutrient, expressed in grams or in percent of calories and log-transformed. The other covariates in the model were considered to be measured without error and included age at diagnosis, study site, race, education, alcohol consumption, years of oral contraception use, smoking status and BMI. The validation study could only generate nutrient data, therefore correction procedures were possible for nutrients but not for food groups.

Results

There was no association between intake of energy and risk of disease in this group of women (Table 1). Results for macronutrients, either as absolute intake in grams or as a percent of calories, also indicated no associations with risk of disease. Results were similar with and without adjustment for energy (not shown). In addition, there were no associations between intake of saturated fat, linoleic acid, or cholesterol and risk of disease. Using data from the 12 days of dietary intake from the validation study, error correction methods revealed no substantive changes in the risk estimates for energy, or any of the macronutrients expressed in grams or percent of calories. For example, in the full model including energy, comparison of the 87.5th percentile to the 12.5th percentile (reference group) of percent of calories from carbohydrates (percent carbohydrates) revealed an uncorrected OR = 0.94 (95% CI = 0.75–1.18) and a corrected OR = 0.89 (95% CI = 0.63–1.27). Similarly, odds ratios for percent fat and percent protein were not statistically significant and changed from 1.08 to 1.15 and 0.89 to 0.73, respectively, with measurement error correction.

A variety of food groups in relation to breast cancer are presented in Table 2. No associations were evident for intake of meat, red meat, fish and poultry, dairy, foods high in animal fat, or high-fat snacks/desserts. However, intake of sweet foods more than 2.8 times per week was associated with increased risk of breast cancer, with associations being greater after adjustment for energy (OR = 1.32, 95% CI = 1.0–1.8 for fourth compared with first quartile). The odds ratios increased in a linear fashion with a significant test for trend ($p = 0.02$). Evaluation of the sweet food group indicates that the major contributors to this food group, by percent contribution to the total weekly frequencies for all subjects, were regular cola soft drinks (18.8%); chocolate candy (13.0%); cake, brownies, and cookies (12.6%); Kool-Aid and fruit drinks (10.3%); non-cola sodas with sugar (9.3%); ice cream (8.2%); and doughnuts & pastries (6.8%). Creation of three new food groups composed of caffeinated sodas, non-caffeinated sodas and drinks, and all sodas and drinks together did not reveal any unique risk related to soft drinks (Table 3). Evaluation of cola versus non-cola drinks also did not identify a group distinctively related to risk (data not shown). In an effort to evaluate risk related to other food groupings of the sweet items, two other food groups were created from the other major contributors to the food group: (1) chocolate candy, chocolate cake, brownies, and cookies; and (2) these items plus ice cream and doughnuts & pastries. These analyses also did not reveal a strong contributor or source of the increased risk for the sweets food group (data not shown).

Although it was not possible to clearly separate foods high and low in *trans*-fatty acids in the sweets food group, it was possible to form a food group high in these fatty acids to evaluate whether this dietary constituent was related to breast cancer. Evaluation of foods from the high-fat snacks and desserts group that would be high in *trans*-fatty acids (*e.g.*, margarine, French fries, doughnuts & pastries) versus those not high in these fatty acids did not reveal any increased risk related to *trans*-fats (data not shown). Further evaluation of percent of calories from the sweets group revealed results similar to the frequency variable in Table 2 (adjusted OR = 1.04, 1.22, 1.27 for quartiles 2, 3, 4). In this analysis, increased risk in the highest quartile represented >13% of calories from sweets compared with <4.7% in the lowest quartile. In an effort to further refine the frequency analysis we incorporated serving size into the sweets food group to show total servings per week. This analysis, adjusted for energy, also suggested increased risk for all quartiles above the reference of <2.5 servings per week (OR = 1.17, 1.21, 1.18 for quartiles 2, 3, 4).

Results for eating patterns are presented in Table 4. Risk did not vary by the number of meals consumed per day. There were insufficient numbers of women reporting four or more meals per day to evaluate this group separately. Reduced risk estimates were noted for women who reported frequent snacking each day; however, none of the estimates was statistically significant (p for trend = 0.09) and adjustment for calories did not alter the association. There were too few women who reported no snacking or minimal snacking (none to four per week) to evaluate this group separately (13 cases and 28 controls). There was a suggestion of reduced risk for women who consumed six or more meals and snacks per day compared with women who had only one or two eating events per day.

Eating away from home, either in a restaurant, cafeteria, or lunch wagon four to seven times per week was associated with a slight increase in risk of disease (p for trend = 0.21). Further adjustment for calories or the sweets food group did not change the associations between eating away from home and risk of disease. In addition, the odds ratios for the sweets food group were not influenced by adjustment for eating in restaurants.

Results for women with *in-situ* disease did not differ from those for women with localized disease for any of the analyses presented. For the sweets group, the odds ratios for the fourth *vs* the first quartile were 1.53 (95% CI = 1.0–2.5) for *in-situ* disease and 1.26 (95% CI = 0.9–1.8) for localized disease. The risk related to the sweets group was evaluated within strata of selected risk factors, which were divided into low- and high-risk

Table 1. Odds ratios for quartiles of calories, macronutrients and fat subtypes among early-stage breast cancer cases <45 years of age

Dietary factor (daily intake)	Cases (n = 568)	Controls (n = 1451)	OR[a] (95% CI)
Total energy (kcal)[b]			
<1129	151	363	1.00
1129–1455	143	363	0.92 (0.7–1.2)
1456–1830	123	363	0.81 (0.6–1.1)
≥1831	151	362	1.03 (0.8–1.4)
Carbohydrates (g)			
<120	153	363	1.00
121–158	136	363	0.84 (0.6–1.1)
159–202	135	363	0.85 (0.6–1.2)
≥203	144	362	0.95 (0.6–1.5)
Fat (g)			
<45	159	363	1.00
45–61	140	363	0.89 (0.7–1.2)
62–83	118	363	0.78 (0.6–1.1)
≥84	151	362	1.01 (0.6–1.6)
Protein (g)			
<46	156	363	1.00
46–58	141	364	0.84 (0.6–1.1)
59–74	139	362	0.80 (0.6–1.1)
≥75	132	362	0.77 (0.5–1.2)
Percent calories from carbohydrates			
<38.8	142	363	1.00
38.8–43.4	149	363	1.07 (0.8–1.4)
43.5–48.6	129	364	0.88 (0.7–1.2)
≥48.7	148	361	1.02 (0.8–1.4)
Percent calories from fat			
<33.8	158	363	1.00
33.8–38.7	115	363	0.79 (0.6–1.1)
38.8–43.3	136	363	0.95 (0.7–1.3)
≥43.4	159	362	1.10 (0.8–1.5)
Percent calories from protein			
<14.6	154	363	1.00
14.6–16.4	145	364	0.96 (0.7–1.3)
16.5–18.3	133	364	0.91 (0.7–1.2)
≥18.4	136	360	0.91 (0.7–1.2)
Saturated fat (g)			
<15.3	154	363	1.00
15.3–20.9	142	363	0.96 (0.7–1.3)
21.0–28.7	124	363	0.88 (0.6–1.2)
≥28.8	148	362	1.09 (0.7–1.7)
Linoleic acid (g)			
<7.8	155	364	1.00
7.8–11.5	143	362	0.91 (0.7–1.2)
11.6–16.5	130	363	0.83 (0.6–1.1)
≥16.6	140	362	0.86 (0.6–1.3)
Cholesterol (mg)			
<145	159	363	1.00
145–199	139	363	0.89 (0.7–1.2)
200–262	127	363	0.82 (0.6–1.1)
≥263	143	362	0.92 (0.6–1.3)

[a] Odds ratios adjusted for age at diagnosis, study site, race, education, alcohol consumption, years of oral contraceptive use, smoking status, BMI, and energy.

[b] Not adjusted for energy.

categories based on previous analyses [10–12]. There was no modification of the effect of the sweets group by BMI (BMI <22 and BMI 22+) or by alcohol intake, although there were few women in the high-alcohol group (14+ drinks/week) for evaluation. Risk of breast cancer was somewhat strong among those who had a

Table 2. Odds ratios for quartiles of food groups among early-stage breast cancer cases <45 years of age

Food group (times per week)	Cases (n = 568)	Controls (n = 1451)	OR[a]	OR[b] (95% CI)
Meat				
<5.6	171	386	1.00	1.00
5.6–7.6	122	345	0.79	0.80 (0.6–1.1)
7.7–10.4	144	374	0.88	0.89 (0.7–1.2)
≥10.5	131	346	0.88	0.85 (0.6–1.2)
Red meat				
<4.2	187	454	1.00	1.00
4.2–6.2	159	396	0.95	0.96 (0.7–1.3)
6.3–8.3	112	289	0.97	0.98 (0.7–1.3)
≥8.4	110	312	0.88	0.84 (0.6–1.2)
Fish & Poultry				
<2.1	155	405	1.00	1.00
2.1–3.4	151	411	0.92	0.93 (0.7–1.2)
3.5–4.8	113	287	0.98	0.99 (0.7–1.3)
≥4.9	149	348	1.08	1.10 (0.8–1.5)
Dairy				
<7.0	162	414	1.00	1.00
7.0–11.8	116	341	0.87	0.89 (0.7–1.2)
11.9–19.5	163	351	1.19	1.23 (0.9–1.6)
≥19.6	127	345	0.97	1.00 (0.7–1.4)
Foods high in animal fat				
<8.4	178	423	1.00	1.00
8.4–11.8	143	356	0.98	1.01 (0.8–1.4)
11.9–16.7	117	329	0.88	0.89 (0.6–1.2)
≥16.8	130	343	0.96	0.92 (0.6–1.3)
High-fat snacks & desserts				
<2.8	150	379	1.00	1.00
2.8–4.8	134	357	0.97	1.00 (0.7–1.3)
4.9–8.3	147	408	1.03	1.07 (0.8–1.4)
≥8.4	137	409	0.98	0.98 (0.7–1.4)
Sweets				
<2.8	160	463	1.00	1.00
2.8–4.8	114	281	1.16	1.21 (0.9–1.6)
4.9–9.7	154	370	1.20	1.28 (1.0–1.7)
≥9.8	140	337	1.24	1.32 (1.0–1.8)

[a] Odds ratios adjusted for age at diagnosis, study site, race, education, alcohol consumption, years of oral contraceptive use, smoking status, and BMI.
[b] Further adjusted for energy.

mother or sister diagnosed with breast cancer (OR = 1.77, 1.78, 1.83, for quartiles 2, 3, 4) than among women without a family history of breast cancer (OR = 1.12, 1.18, 1.26 for quartiles 2, 3, 4). None of these results was statistically significant, however, and a limited number of subjects (85 cases and 94 controls) with a family history of breast cancer make interpretation of these results difficult.

Discussion

Risk of breast cancer was not associated with macronutrients and most food groups. No association was observed for total fat or type of fat in this investigation. Error correction also did not reveal any risk associated with fat intake. Although summary analyses of case–control studies had shown an association for total fat [19, 20], saturated fat [20], and monounsaturated fat [20], analyses of pooled cohort studies have not demonstrated an association for total fat [2, 19, 21] or for types of fat [21]. Of particular interest, consistent with our findings, is the lack of association for total [20, 21], saturated [21], or animal fat [21] with premenopausal breast cancer risk. Thus, in general, the data do not support a role of total fat or types of fat with risk of premenopausal breast cancer.

We observed a consistent association between the intake of sweet items and risk of early-onset breast cancer, whether expressed as frequency of intake,

Table 3. Odds ratios for quartiles of different types of full-sugar soft drinks from the sweets food group among early-stage breast cancer cases <45 years of age

Type of soft drink (times/week)	Cases (n = 568)	Controls (n = 1451)	OR[a] (95% CI)
Caffeinated soft drinks[b]			
None	354	894	1.00
≤0.7	104	264	1.05 (0.8–1.4)
2.8	52	132	1.07 (0.7–1.5)
≥5.6	58	158	1.00 (0.7–1.4)
Non-caffeinated drinks[c]			
None	287	771	1.00
≤0.7	90	214	1.20 (0.9–1.6)
1.4–3.5	103	246	1.20 (0.9–1.6)
≥4.2	86	220	1.13 (0.8–1.6)
Full-sugar drinks[d]			
None	233	607	1.00
0.7–1.4	120	295	1.08 (0.8–1.4)
2.1–5.6	105	272	1.04 (0.8–1.4)
≥6.3	110	277	1.09 (0.8–1.5)

[a] Odds ratios adjusted for age at diagnosis, study site, race, education, alcohol consumption, years of oral contraceptive use, smoking status, BMI, and energy.
[b] Regular colas with sugar and caffeine.
[c] Caffeine-free sodas with sugar, other sodas with sugar, Hi-C or other vitamin C fortified fruit drinks.
[d] Caffeinated and non-caffeinated drinks combined.

Table 4. Odds ratios for quartiles of number of meals and snacks among early-stage breast cancer cases < 45 years of age

Dietary factor	Cases (n = 568)	Controls (n = 1451)	OR[a] (95% CI)
Meals per day			
1	154	422	1.00
2	252	584	1.16 (0.9–1.5)
3+	162	443	0.98 (0.7–1.3)
DK[b]	0	2	
Snacks			
0–7/week	272	619	1.00
2/day	190	521	0.86 (0.7–1.1)
3/day	77	214	0.85 (0.6–1.2)
4–6+/day	26	86	0.74 (0.5–1.2)
DK	3	11	
Meals + snacks			
1–2/day	76	188	1.00
3/day	168	411	0.97 (0.7–1.4)
4/day	177	428	1.01 (0.7–1.4)
5/day	104	271	0.96 (0.7–1.4)
6+/day	38	137	0.69 (0.4–1.1)
DK	5	16	
Eating away from home			
< 1/week	148	427	1.00
1–3 times/week	227	572	1.13 (0.9–1.5)
4–7 times/week	184	418	1.19 (0.9–1.6)
Never + DK	9	34	

[a] Odds ratios adjusted for age at diagnosis, study site, race, education, alcohol consumption, years of oral contraceptive use, smoking status, and BMI.
[b] DK = do not know.

servings per week, or percent of calories as sweets. It is noteworthy that there was no association with carbohydrates in these analyses; in fact, many studies have not evaluated different types of carbohydrates because of the lack of a main effect of the macronutrient. Few studies have evaluated carbohydrates and/or carbohydrate components. No associations have been observed between breast cancer risk and intake of sucrose [22, 23], sugar [24, 25], starch [22, 24], and sweet desserts [26]. Other investigators report increased risk related to particular foods or food groups high in sugar, but often evaluated many foods and did not focus on the finding related to the sweet items. Increased risks were reported for sweet desserts [27], pastries [28], desserts and chocolate [29], sugar & candies [30], cake & desserts [31], and refined sugar [31]. The discrepancies in findings for studies of carbohydrate subgroups and those with foods may relate to exposure assessment and classification. Some studies may have had few line items for sweet foods, whereas others may have had more items, which more clearly described the exposure. Further, use of food composition tables to assess dietary constituents may introduce error obscuring an association, or may not focus on the exposure associated with risk.

The inconsistencies in the literature on the relation of sugars and breast cancer risk have been noted previously. In a review of the topic, Burley [32] suggested that only studies that described the exposure as foods high in sugars were associated with risk. Studies that described the exposure as sucrose, as quantified from food composition tables, did not show increased risk. However, there were no studies that quantified both. These foods high in sugar are often also high in *trans*-fatty acids and therefore the exposure of interest could be the type of fat and not the sugar content. The possibility of an effect due to *trans*-fatty acids in our data cannot be excluded, although our *post-hoc* analyses did not support this association. Breaking down the sweets group did not identify foods or groups of foods that were strongly associated with risk. The non-soda food group was rich in *trans*-fatty acids and high in simple sugars. Therefore, we would have anticipated an increased risk in this group if *trans*-fatty acids were important. Misclassification could have produced our results, however. With the lack of a *trans*-fatty acid database it is difficult to assess and quantify this exposure. Our results indicate that a common ingredient in the sweets food group was associated with risk, and argues against an association of *trans*-fatty acids. However, further evaluation of this issue with food

composition data, which may be available in the near future, is warranted.

Our data suggest that a common constituent in the sweets food group was associated with increased risk, not a particular food or nutrient subgroup driving the association. Thus, high exposure to simple sugars may be the ingredient associated with increased risk of breast cancer among young women. Intake of simple sugars would result in insulin secretion. Although we do not have a measure of glycemic index or insulin-inducing capacity of the diet, our results are consistent with hypotheses suggesting increased breast cancer risk related to high exposure to insulin [33] and insulin resistance [34–36]. Insulin has been linked to increased biologic activity of insulin-like growth factor I (IGF-I) [33]. Both insulin and IGF-I can stimulate cell proliferation and inhibit apoptosis, promoting tumor growth [33]. Further, insulin resistance can lead to elevated androgen and estrogen concentrations because insulin stimulates ovarian steroid secretion [33, 37, 38].

Analytic epidemiologic studies support a role for insulin and IGF-I and early-onset breast cancer. Premenopausal breast cancer has been associated with elevated concentrations of insulin or c-peptide in some [39, 40] but not all studies [41]. Insulin resistance, as measured by fasting glucose and after a glucose load, was not related to breast cancer in one prospective study [42]. This study, however, did not have many early-onset breast cancers. In premenopausal women, IGF-I has been shown to be associated with breast cancer [41, 43–46] and with breast density [47]. IGF-I has been associated with premenopausal breast cancer and breast density but not with postmenopausal disease [41, 44, 45, 47]. Although relatively little is known about the determinants of IGFs in well-nourished populations [48], there is an integration and concordance in circulating levels of IGFs and insulin [33], suggesting a link to similar dietary factors.

Our results for eating patterns were weak but suggest possible associations related to number of snacks plus meals per day. Women who reported frequent eating events may be at reduced risk of breast cancer. Frequent consumption of foods may stabilize glucose levels over the course of the day and not create spikes of glucose concentrations following large meals and the ensuing challenge to the insulin response. Eating out of the home may be associated with increased risk but our results were limited by few women in the high category of 7+ times per week. These results warrant replication in other studies.

These data indicate increased risk of early-onset breast cancer associated with high consumption of foods high in sucrose. Although this sweets food group was not hypothesized to be associated with risk *a priori*, the consistency of the results in these data and with an insulin-related biologic mechanism make it a compelling finding. Data suggestive of reduced risks for frequent meals and snacks are also consistent with an insulin-related mechanism. Alternatively, the sweets food group could be identifying a dietary pattern that indicates substitution of sweet foods for other foods, or an entire pattern of eating that would be related to risk of disease. Our data are restricted to breast cancer in women <45 years of age with *in-situ* or localized disease. Further studies are warranted to evaluate this risk factor in all stages of pre- and postmenopausal breast cancer.

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Appendix

Line items comprising food groups

MEAT
Bacon
Sausage
Hamburgers
Beef steaks, roasts
Beef stew
Liver
Pork
Fried chicken
Chicken or turkey
Spaghetti
Hot dogs
Ham, bologna
Veal, lamb
Chili with beans
Beef pot pie

RED MEAT
Bacon
Sausage
Hamburgers
Beef steaks, roasts
Beef stew
Liver
Pork
Spaghetti
Hot dogs
Ham, bologna
Chili with beans
Beef pot pie

FISH & POULTRY
Fried chicken
Chicken or turkey
Tuna
Shellfish
Fried fish
Other fish
Squid

DAIRY
Milk on cereal
Dishes with cheese
Low fat cottage cheese
Cottage cheese
Cheese and cheese spreads
Lowfat yogurt
Regular yogurt
Ice cream
Lowfat frozen yogurt
Whole milk
2% Milk
Skim Milk
Sour cream
Custard
Fat-free ice cream
Cream cheese, soft cheese

ANIMAL FAT
Bacon
Sausage
Hamburgers
Beef steaks, roasts
Beef stew
Liver
Pork
Fried chicken
Spaghetti
Hot dogs
Ham, bologna
Chili with beans
Beef pot pie
Gravies made with meat drippings
Eggs
Pizza
Mixed dishes w cheese
Regular cottage cheese
Other Cheeses
Regular yogurt
Ice Cream
Whole Milk
Cream/half-half in coffee
Cream soups
Custard
Cream cheese, soft cheese

HIGH-FAT SNACKS AND DESSERTS
French Fries
Potato chips, corn chips, popcorn
Peanuts
Other nuts and seeds
Ice Cream
Pies (other than pumpkin)
Doughnuts, pastry
Chocolate cake, brownies, cookies
Chocolate Candy

SWEETS
Ice Cream
Pies (other than pumpkin)
Doughnuts, pastries
Chocolate cake, brownies, cookies
Chocolate Candy
Sugar for coffee, cereal
Lowfat frozen yogurt
Kool-Aid, Hi-C, fortified fruit drinks with vitamin C
Waffles, pancakes
Hot Chocolate
Honey/Molasses
Juice Sparklers
Custard
Fat-free ice cream, other similar fat-free frozen desserts
Jello or sherbet
Candy (non-chocolate)
Regular colas with sugar
Caffeine-free regular soda
Other sodas w/sugar